REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office Action dated August 26, 2010 is respectfully requested in view of this amendment. By this amendment, claims 11, 13-16 and 18 were cancelled and claims 1 and 12 have been amended. Claims 1-5, 12 and 17 are pending in this application and presented for examination.

Claim 1 was amended to clarify the features of altering a light path passing through at least one end of the optical waveguide and providing a uniform intensity of light, an infra-red cutting filter filtering light transmitted through a light path that comprises the filter, a reflective mirror and an optical waveguide, illuminating the sample with a uniform light intensity distribution as provided by the uniform intensity of light from the optical waveguide, and receiving fluorescence irradiated from the sample by that light. Claim 12 was amended to describe the reflective mirrors. Support is found in the original specification, *inter alia*, at page 8 line 19 – page 9 line 5, corresponding to paragraphs [0051] and [0052] (as published in U.S. Published Application No. 2006-0145098) and page 10 line 19 – page 11 line 2, corresponding to paragraph [0057]. It is respectfully submitted that the above amendments introduce no new matter within the meaning of 35 U.S.C. §132.

ACKNOWLEDGEMENT OF INTERVIEW

An interview, granted by the Examiner and held on November 8, 2010, is gratefully acknowledged. During the interview, claims 1 and 11 were discussed. The applicability of the prior art references were discussed, as related to the specific optical elements and the arrangement of the optical elements. In the interview, it was agreed that the applicant would submit an amended claim which would positively describe the structure of the claimed apparatus.

The interview is believed to have expedited the prosecution of this case, and the Examiner's extra efforts in this regard are appreciated.

Rejections Under 35 U.S.C. §103

In the outstanding Office Action, the Examiner rejected claims 1-5 and 11-18 under 35 U.S.C. §103(a) as being unpatentable over Applicant's Admitted Prior Art in view of U.S. Patent No. 4,076,420 to De Maeyer, et al. (hereinafter *De Maeyer*). Applicant's description of the art includes a real-time monitoring apparatus for a biochemical reaction in which a temperature control block comprising a thermoelectric element, a heat transmission block, a light irradiation source comprising a lamp with a first ellipsoidal reflecting mirror or a parabolic mirror and a condensing lens are used with an optical system comprising a receiving part. *De Maeyer* is cited as teaching optical detection using a light source which provides light which is focused with a series of lenses, passed through a monochromator, a flexible light pipe, a series of optics to a cell chamber, and detected with a series of detectors.

Response

This rejection is traversed as follows. To show obviousness under §103, it is necessary to show an incentive to benefit from the change. *KSR International Co. v. Teleflex Inc. et al.*, 127 S.Ct. 1727, 82 USPQ2d 1385 (2007).

> "The proper question to have asked was whether a pedal designer of ordinary skill, facing the wide range of needs created by developments in the field of endeavor, would have seen a benefit to upgrading Asano with a sensor. In automotive design, as in many other fields, the interaction of multiple components means that changing one component often requires the others to be modified as well." (*id* at 127 S.Ct. 1744)

A demonstration of obviousness under §103 requires that the combination represent a design step well within the grasp of a person of ordinary skill in the relevant art. *id.*

> "KSR provided convincing evidence that mounting a modular sensor on a fixed pivot point of the Asano pedal was a design step well within the grasp of a person of ordinary skill in the relevant art. (*id* at 127 S.Ct. 1746)

The standard for anticipation under 35 USC 102 and obviousness under 35 USC 103(a) following KSR is detailed in *Forest Labs v. Ivax Pharmaceuticals*, 127 S.Ct. 1727,

82 USPQ2d 1385 (2007). In *Forest Labs*, the court determined that a reference mentioned a particular chemical component, but did not explain how to obtain it and therefore deemed that, "A reference that is not enabling is not anticipating." The court then deemed the product was therefore unobvious over that reference.

Applicants' claim 1, as amended, describes:

> "... an optical waveguide ... having a configuration that alters light path passing through ... the optical waveguide and provides a uniform intensity of light, an infra-red cutting filter filtering light transmitted through a light path that comprises said infra-red cutting filter, said reflective mirror and the optical waveguide ... a selective transmission filter ..., said light illuminating the sample with a uniform light intensity distribution as provided by the uniform intensity of light from the optical waveguide, and a condensing lens positioned outside ... [the] light path ... the fluorescence irradiated from the sample by the light emitted from the light irradiation source as transmitted through a light path comprising the optical waveguide, the selective transmission filter and the condensing lens."

Accordingly, Applicants' claims set forth an apparatus which features:

1. a temperature control block comprising a thermoelectric element and a heat transmission block;
2. a light irradiation source and an infra-red cutting filter;
3. an optical waveguide providing uniform intensity of light as reflected through a reflective mirror;
3. an optical system comprising receiving part outside of the light path of the infra-red cutting filter; and
4. the fluorescence irradiated from the sample transmitted through a light path comprising the optical waveguide, the selective transmission filter and the condensing lens.

In contrast, the apparatus described by *De Maeyer* contains:

1. a sample cell unit EZ comprising a thermostat EH;
2. a series of excitation units comprising unit ET for the temperature-jump and/or the field-jump method, unit EP for the pressure-jump and/or the flow method and unit EF for the flashlight pulse method;
3. an illumination unit EM; and
4. a series of photodetectors connected to a signal processing unit ED.

This is set forth in *De Maeyer*'s specification:

"FIG. 1 shows a simplified diagram of the new apparatus which contains:
"1. A sample cell unit EZ for inserting sample cells Z of similar outer shape designed for different mixing and relaxation measurements. These cells are inserted into a holder HZ allowing easy changing, good reproducible positioning and the supply of various perturbation energies. The sample cell unit comprises also optical elements such as lenses, fllters and polarizers according to the optical parameter of observation. A thermostat EH is also provided.
"2. A series of excitation units: A unit ET for the temperature- jump and/or the field-jump method comprising a high voltage power supply 1.1, a charging resistor 1.2, a high voltage capacitor 1.3 (preferably interchangeable) which may also be constructed as a coaxial cable, a spark gap 1.5, an additional resistance 1.6 which can be adapted to the characteristic impedance of the coaxial cable, and a high voltage connection 1.7 to the sample cell holder HZ. A unit EP for the pressure-jump and/or the flow method comprising a compressed air reservoir 1.10 with reducing valves 1.11, magnetic control valves 1.12, a schematically simplified control circuit 1.13, and suitable connections for compressed air.
"A unit EF for the flashlight pulse method comprising a flashlamp QF with a power supply 1.15 and an ignition circuit 1.16.
"3. An illumination unit EM for generating one or more high intensity monochromatic light beams.
"4. A series of photodetectors 01,02,03,04,01/,02'connected to a signal processing unit EO."
(*De Maeyer* at column 5, line 55 to column 6, line 19. See also Fig. 1 of *De Maeyer*.)

That is, *De Maeyer* describes operation with additional components such as a series of excitation units, which components are not required in the apparatus claimed by Applicants.

Moreover, the apparatus as claimed by Applicants comprises only one photodetector, whereas *De Maeyer* has described multiple photodetectors. In one example, *De Maeyer* uses at least 4 photodetectors D1, D2, D3 and D4 and additional photodetector D1' and D2':

> D = photodetector, general
> D1 = reference photodetector
> D2 = absorption photodetector
> D3,D4 = photodetectors in the secondary lightpath
> D1',D2' = additional photodetectors
> (See *De Maeyer* at column 4, lines 64-67.)

Therefore, the basic configurations of *De Maeyer* and the Applicants' claimed apparatus are structurally and functionally different from one another.

Applicant's description of the art is acknowledged as not describing a rectangular or round optical waveguide or a focusing lens. *De Maeyer* is cited as showing optical detection using a light source which provides light which is focused with a series of lenses, passed through a monochromator, a flexible light pipe, a series of optics to a cell chamber, and detected with a series of detectors. Instead, the rejection under 35 USC §103(a) alleges that it would have been obvious to combine *De Maeyer*'s detectors so as to provide light samples to the cells. This stipulation fails to meet the *KSR* test because the combination of irradiation by light with uniform intensity to sample contained in the reaction tubes, using a condensing lens and the optical waveguide, and receiving fluorescence irradiated from the sample by the light emitted from the light irradiation source is not a mere design step (not "a design step well within the grasp of a person of ordinary skill in the relevant art"). In this regard, *De Maeyer* specifies that multiple detectors are used in combination with additional components such as excitation units and therefore fails to suggest Applicants' claimed features. This is more than a superficial difference; it is a basic function of the *De Maeyer* operability.

In addition, the light pipe of *De Maeyer* has the structure in which both ends of the pipe are connected to the movable exit slits, whereas the light waveguide as recited in Applicants' claims has an open structure, with lens and refractive mirror located at both ends of the light waveguide. By adopting this structure, Applicants can minimize the size of light waveguide and

can fit the light size with corresponding reaction plate size. This is substantially distinct from *De Maeyer* because, in order to apply the light pipe of *De Maeyer* to the apparatus as claimed by Applicants, the size of light pipe should be as large as that of the actual reaction plate, for example, a 96-well plate. That is, such a flexible light tube of *De Maeyer* having the size required for use in Applicants' claimed apparatus is technically not achievable.

It is further pointed out that the light waveguide as claimed by Applicants is used to provide uniform light intensity, thereby providing a capability of monitoring the biological reaction progress with uniform sensitivity over the whole reaction plate area. This is distinguished from the *De Maeyer* apparatus in that the light pipe of *De Maeyer* is used simply for light transmission. That is, with reference to the detailed description of *De Maeyer*, when the light source A' and the monochromator M' is omitted in Fig. 3, flexible UV-transmitting light-pipe G is connected between movable exit slit and monochromator slit S', using the light pipe as a light path:

> "The light source A' and the monochromator M' can be omitted in FIG. 3 if the monochromator M is provided with a second exit slit which can be moved with respect to the fixed exit slits singular form to give the light of wavelength 11.2, A flexible UV-transmitting light-pipe G (broken lines) is connected to the movable exit slit and directed into the right-side light path at the place of the monochromator slit S'. Monochromators according to Czerny-Turner without internal deflection mirrors (see FIG. 1) are especially suitable for this purpose. The entrance aperture of the light-pipe itself can serve as the
>
> additional monochromator exit. For sample cells with a round entrance aperture the waveguide G may furthermore transform a rectangular cross section into a round one." (*De Maeyer* at column 9, lines 20-34. See also Fig. 3 of *De Maeyer*.)

From this, it is clear that the roles of the light waveguide as claimed by Applicants and the light pipe of *De Maeyer* are fundamentally different. It is therefore submitted that the light waveguide as claimed by Applicants are neither shown nor suggested by the light pipe of *De Maeyer*.

Moreover, a real-time monitoring apparatus as set forth in Applicants' claims uses a light irradiation source comprising a lamp and an optical waveguide to irradiate uniform light into a

sample within a reaction tube. The light in the light waveguide is propagated by means of total internal reflection. Consequentially, the light beam at the end of the light waveguide provides a uniform two-dimensional light source. By using the uniform light beam, the reaction progress may be more easily measured over the whole range of the reaction tube. This is explained in detail by Applicants at paragraph [0051] (as published in U.S. Published Application No. 2006-0145098), as well as Applicants' Fig. 3. Paragraph [0051] states:

> "The light from the light radiation lamp (5) is focused into the light waveguide (8). The light in the light waveguide is propagated in a manner of total internal reflection. The light beam at the end of the light waveguide (8) become a uniform 2-dimensional light source and are focused on the samples contained in the reaction tubes (4) through the first condensing lens (10). By using the uniform light beam (31), there reaction progress may be more easily measured over the whole range of the reaction tubes."

This is set forth in Applicants' claim 1:

> "... provides a uniform intensity of light... , said light illuminating the sample with a uniform light intensity distribution as provided by the uniform intensity of light from the optical waveguide ... ."

By use of the claimed structure, Applicants are able to provide a uniform light intensity such that at the edges of reaction tube plate has more than 85% of light intensity in the center of reaction tube plate by using the apparatus. This is also explained in detail in Applicants' paragraph [0068], which states:

> "As shown in FIG. 3, a plane wave light source of the present invention with uniformly distributed intensity over the cross-section of light beam has more than 85% (21) of light intensity at the edges compared with the light intensity in the center of reaction tube plate (34) and enables to monitor the reaction progress more uniformly by achieving substantially improved light intensity uniformity compared with the prior art."

This feature substantially distinguishes Applicants' claimed apparatus over that of the cited references. Applicants' arrangement avoids a situation in which light intensity at the edges of the plate would likely be about 50-60% of that in the center. In other words, as explained in Applicants' paragraph [0061],

> "... analysis has been made by adjusting the measured light intensity to the light intensity at the edges. This brings the sensitivity of the whole apparatus degraded. In addition, in case of using a ultra-sensitivity light receiving element to overcome the degradation problem of sensitivity, the apparatus requires the increase in size and costs."

Accordingly, the apparatus as set forth in independent claim 1 has a simplified and practical structure compared to that of *De Maeyer*. In particular, *De Maeyer* does not show or suggest Applicants' light waveguide. Therefore, since the configuration and reaction mechanism as claimed by Applicants and the function of Applicants' claimed apparatus are fundamentally different from those of *De Maeyer*, it is respectfully submitted that there is no suggestion in the prior art of record to construct Applicants' claimed apparatus. Further, it is respectfully submitted that there is no suggestion of Applicants' claimed subject matter even in view of *De Maeyer* in combination with Applicants' Figs. 2 and 5.

Applicants therefore respectfully submit that Applicant's description of the art taken in view of *De Maeyer* does not fairly teach or suggest all the features as recited in claim 1. It is therefore respectively submitted that the rejection under 35 U.S.C. 103(a) should be withdrawn.

Claims 2 5, 12 and 17

Claims 2-5, 12 and 17 are written in dependent form and depend from claim 1. Those dependent claims should be allowable for at least the same reasons that claim 1 is allowable.

CONCLUSION

In light of the foregoing, Applicants submit that the application is in condition for allowance. If the Examiner believes the application is not in condition for allowance, Applicants respectfully request that the Examiner call the undersigned.

Respectfully submitted,
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